

**Amendments to the Claims**

This listing of claims will replace all prior versions, and listings, of claims in this application.

The following amendments do not constitute an admission regarding the patentability of the amended subject matter and should not be so construed. Amendments to the claims were made for purposes of more clearly stating the claimed subject matter and do not add new matter or alter the scope of the claims.

**Listing of Claims:**

1. (Previously presented) A method for constructing a gene network of relationships between a plurality of genes of a set of genes and generating a graph representing the gene network of relationships between the genes comprising the steps of:

(a) providing a quantitative time course data library for the set of genes of an organism, said library including expression results based on time course of expression of each gene in said set of genes, wherein the expression results comprise gene expression data at a plurality of time points for each gene in said set of genes, quantifying an average effect on expression of each gene at each time point by each other of said genes at each time point, and quantifying a measure of variability of the effect on expression of each gene at each time point on each other of said genes;

(b) creating a gene expression matrix from said library, wherein the gene expression matrix comprises matrix data comprising the effects on expression of each gene at each time point by each other of said genes at each time point;

(c) applying a Bayesian computational model to the matrix data, wherein said Bayesian model comprises minimizing a BNRC<sub>dynamic</sub> criterion; and

(d) generating the gene network of relationships between said genes and generating a graph representing the gene network of relationships between said genes.

2. (Canceled)

3. (Previously presented) The method of claim 1, wherein said step of minimizing a BNRC<sub>dynamic</sub> criterion comprises using a non-linear curve fitting method selected from the group consisting of polynomial bases, Fourier series, wavelet bases, regression spline bases and B-splines.

4. (Previously presented) The method of claim 1, wherein said data library is created by obtaining the gene expression data at the plurality of time points from a time course study studying altering gene expression over time.

5. (Previously presented) The method of claim 1, wherein said step of minimizing said BNRC<sub>dynamic</sub> criterion further comprises selecting a Bayesian mode using a backfitting algorithm.

6. (Previously presented) The method of claim 1, wherein said step of minimizing a BNRC<sub>dynamic</sub> criterion further comprises using Akaike's information criterion.

7. (Previously presented) The method of claim 1, wherein said step of minimizing a BNRC<sub>dynamic</sub> criterion further comprises using maximum likelihood estimation.

8. (Previously presented) The method of claim 1, wherein said plurality of genes are associated with a cell cycle of the organism.

9. (Previously presented) The method of claim 1, wherein said measure of variability is variance.

10. (Previously presented) The method of claim 1, wherein said non-linear curve fitting method is a non-parametric method.

11. (Original) The method of claim 10, wherein said non-parametric method for minimizing a BNRC<sub>dynamic</sub> criterion includes using heterogeneous error variances.

12. (Previously presented) The method of claim 11, wherein said step of minimizing a BNRC<sub>dynamic</sub> criterion further comprises the steps of:

(1) making a score matrix whose (i, j)<sup>th</sup> element is the BNRC<sub>dynamic</sub><sup>j</sup> score of the graph gene<sub>i</sub>→ gene<sub>j</sub>;

(2) implementing one or more of adding the BNRC<sub>dynamic</sub><sup>j</sup> score of the effect of parent gene<sub>i</sub> on gene<sub>j</sub> to a calculation of BNRC<sub>dynamic</sub>, removing the BNRC<sub>dynamic</sub><sup>j</sup> score of the effect of parent gene<sub>i</sub> on gene<sub>j</sub> to a calculation of BNRC<sub>dynamic</sub>, and reversing the BNRC<sub>dynamic</sub><sup>j</sup> score of the effect of parent gene<sub>i</sub> on gene<sub>j</sub> to a calculation of BNRC<sub>dynamic</sub><sub>s</sub> which provides the smallest BNRC<sub>dynamic</sub>; and

(3) repeating step 2 until the BNRC<sub>dynamic</sub> does not reduce further.

13. (Original) The method of claim 11, wherein said step of minimizing a BNRC<sub>dynamic</sub> criterion further comprises the step of applying a hill-climbing algorithm to minimize BNRC<sub>dynamic</sub>.

14. (Previously presented) The method of claim 11, wherein an intensity of an edge is determined using a bootstrap method.

15. (Previously presented) The method of claim 14, wherein said bootstrap method comprises the steps of:

(1) providing a bootstrap gene expression matrix by randomly sampling a number of times, with replacement, from the original gene library expression data;

(2) estimating the gene network for gene<sub>i</sub> and gene<sub>j</sub>;

(3) repeating steps (1) and (2)  $T$  times, thereby producing  $T$  gene networks; and

(4) calculating the bootstrap edge intensity between gene<sub>i</sub> and gene<sub>j</sub> as  $(t_1+t_2)/T$ .

16-17. (Canceled)

18. (Previously presented) The method of claim 1, comprising grouping said genes into one or more equivalence sets.

19. (Canceled)

20. (Previously presented) A method for constructing a gene network model of a system containing a network of genes from time course gene expression data, said method comprising:

applying a Bayesian computational model to the time course gene expression data, wherein applying said Bayesian computational model comprises minimizing a BNRC<sub>dynamic</sub> criterion; and

generating a graph representing the gene network model resulting from applying the Bayesian computational model to the time course gene expression data wherein BNRC<sub>dynamic</sub> criterion is minimized.

21. (Original) The method of claim 20, wherein minimizing the BNRC<sub>dynamic</sub> criterion comprises using a non-linear curve fitting method selected from the group consisting of polynomial bases, Fourier series, wavelet bases, regression spline bases and B-splines.

22. (Previously presented) The method of claim 20, wherein minimizing the BNRC<sub>dynamic</sub> criterion comprises selecting a Bayesian model using a backfitting algorithm.

23. (Original) The method of claim 20, wherein minimizing the BNRC<sub>dynamic</sub> criterion comprises using Akaike's information criterion.

24. (Original) The method of claim 20, wherein minimizing the BNRC<sub>dynamic</sub> criterion comprises using maximum likelihood estimation.

25. (Original) The method of claim 20, wherein minimizing the BNRC<sub>dynamic</sub> criterion comprises using a non-linear curve fitting method, wherein the non-linear curve fitting method is a non-parametric method.

26. (Original) The method of claim 25, wherein the non-parametric method includes using heterogeneous error variances.

27. (Previously presented) The method of claim 26, wherein minimizing the BNRC<sub>dynamic</sub> criterion further comprises the steps of: (1) making a score matrix whose (i, j)<sup>th</sup> element is the BNRC<sub>dynamic</sub> score of the graph gene<sub>i</sub> → gene<sub>j</sub>; (2) implementing one or more of adding the BNRC<sup>j</sup><sub>dynamic</sub> score of the effect of parent gene<sub>i</sub> on gene<sub>j</sub> to a calculation of BNRC<sub>dynamic</sub>, removing the BNRC<sup>j</sup><sub>dynamic</sub> score of the effect of parent gene<sub>i</sub> on gene<sub>j</sub> to a calculation of BNRC<sub>dynamic</sub>, and reversing the BNRC<sup>j</sup><sub>dynamic</sub> score of the effect of parent gene<sub>i</sub> on gene<sub>j</sub> to a calculation of

BNRC<sub>dynamic</sub>, which provides the smallest BNRC<sub>dynamic</sub>; and (3) repeating step 2 until the BNRC<sub>dynamic</sub> does not reduce further.

28. (Previously presented) The method of claim 26, wherein minimizing the BNRC<sub>dynamic</sub> criterion further comprises the step of applying a hill-climbing algorithm to minimize the BNRC<sup>ij</sup><sub>dynamic</sub>.

29. (Previously presented) The method of claim 26, wherein an intensity of an edge is determined using a bootstrap method.

30. (Previously presented) The method of claim 29, wherein said bootstrap method comprises the steps of:

- (1) providing a bootstrap gene expression matrix by randomly sampling a number of times, with replacement, from the original gene library expression data;
- (2) estimating the gene network for gene<sub>i</sub> and gene<sub>j</sub>;
- (3) repeating steps (1) and (2)  $T$  times, thereby producing  $T$  gene networks; and
- (4) calculating the bootstrap edge intensity between gene<sub>i</sub> and gene<sub>j</sub> as  $(t_1 + t_2)/T$ .

31-44. (Canceled)